

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
1 September 2005 (01.09.2005)

PCT

(10) International Publication Number  
**WO 2005/080316 A2**

(51) International Patent Classification<sup>7</sup>: **C07C 233/68**,  
233/77, 63/04, 69/78, A61K 31/167, 31/192, 31/216,  
31/235

(GB). **PRYCE, Gareth** [GB/GB]; Department of Neu-  
roinflammation, Institute of Neurology, University College  
London, 1 Wakefield Street, London WC1N 1PJ (GB).

(21) International Application Number:  
PCT/GB2005/000605

(74) Agents: **CLYDE-WATSON, Zoe** et al.; D Young & Co,  
120 Holborn, London EC1N 2DY (GB).

(22) International Filing Date: 21 February 2005 (21.02.2005)

(81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,  
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,  
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,  
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,  
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,  
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,  
ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
0403864.2 20 February 2004 (20.02.2004) GB

(71) Applicant (for all designated States except US): **UNIVER-  
SITY COLLEGE LONDON** [GB/GB]; Wolfson Institute  
for Biomedical Research, The Cruciform Building, Gower  
Street, London WC1E 6BT (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **OKUYAMA,  
Masahiro** [JP/JP]; Mitsubishi Pharma Corporation, 6-9,  
Hiranomachi, 2 Chome, Chuo-ku, Osaka 541-0046 (JP).  
**SELWOOD, David** [GB/GB]; Wolfson Institute for  
Biomedical Research, University College London, The  
Cruciform Building, Gower Street, London WC1E 6BT  
(GB). **VISINTIN, Cristina** [IT/GB]; Wolfson Institute  
for Biomedical Research, University College London,  
The Cruciform Building, Gower Street, London WC1E  
6BT (GB). **BAKER, David** [GB/GB]; Department of  
Neuroinflammation, Institute of Neurology, University  
College London, 1 Wakefield Street, London WC1N 1PJ

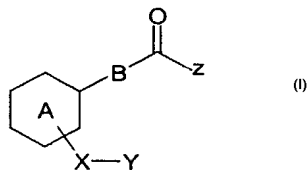
(84) Designated States (unless otherwise indicated, for every  
kind of regional protection available): ARIPO (BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,  
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),  
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,  
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,  
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,  
GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— without international search report and to be republished  
upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: MODULATOR



(57) Abstract: The present invention relates to a compound of formula (I), or a pharmaceutically acceptable salt thereof, wherein Z is OR<sup>1</sup> or NR<sup>1</sup>R<sup>2</sup> wherein each of R<sup>1</sup> and R<sup>2</sup> is independently H, or a hydrocarbyl group; X is an alkylene, alkenylene, or alkynylene group, each of which may be optionally substituted by one or more substituents selected from alkyl, COOH, CO<sub>2</sub>-alkyl, alkenyl, CN, NH<sub>2</sub>, hydroxy, halo, alkoxy, CF<sub>3</sub> and nitro; Y is a polar functional group selected from OH, NO<sub>2</sub>, CN, COR<sup>3</sup>, COOR<sup>3</sup>, NR<sup>3</sup>R<sup>4</sup>, CONR<sup>3</sup>R<sup>4</sup>, SO<sub>3</sub>H, SO<sub>2</sub>-R<sup>3</sup>, SO<sub>2</sub>NR<sup>3</sup>R<sup>4</sup> and CF<sub>3</sub>, where each of R<sup>3</sup> and R<sup>4</sup> is independently H or a hydrocarbyl group; A is an aryl or heteroaryl group, each of which may be optionally substituted; and B is (CH<sub>2</sub>)<sub>n</sub> where n is 0, 1, 2, 3, 4 or 5; with the proviso that: (i) when A is phenyl, n is 0, and Z is OH, X-Y is other than *meta*-C≡C-(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H, *meta*-C≡C-(CH<sub>2</sub>)<sub>2</sub>OH, *meta*-C≡C-(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>Me, *meta*-(CH<sub>2</sub>)<sub>4</sub>CO<sub>2</sub>H, *ortho*-CH<sub>2</sub>CO<sub>2</sub>H, *ortho*-(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H and *ortho*-(CH<sub>2</sub>)<sub>4</sub>CO<sub>2</sub>H; and (ii) when A is phenyl, n is 0, and Z is OMe, X-Y is other than *meta*-C≡C-(CH<sub>2</sub>)<sub>4</sub>OH. Further aspects of the invention relate to the use of such compounds in the preparation of a medicament for the treatment of a muscular disorder, a gastrointestinal disorder, or for controlling spasticity or tremors.



WO 2005/080316 A2